

4115-178

**SECTION I**  
**AMENDMENTS TO THE SPECIFICATION**

**Please amend the specification as follows:**

**At page 8, lines 15-36, please insert the following replacement paragraph:**

mRNA molecules lacking a 5' cap modifier, which is normally added in the nucleus to nuclear mRNA transcripts and enhances ribosome recognition, are poorly translated in eukaryotic cells unless an IRES sequence is present upstream of the gene of interest. The particular IRES employed in the present invention is not critical and can be selected from any of the commercially available vectors that contain IRES sequences. Thus, IRES sequences are widely available and can be obtained commercially from plasmid pIRES2-EGFP (Clontech; [44]) by PCR using primers specific for the 5' and 3' ends of the IRES located at nucleotides 665-1251 in pIRES2-EGFP. The sequences in plasmid pIRES-EGFP can be obtained from the manufacturer (at hypertext transfer protocol world wide web address <http://www.clontech.com/techinfo/vectors/vectorsF-I/pdf/pIRES2-EGFPseq.pdf>). An similar IRES can also be obtained from plasmid pCITE4a (Novagen, Madison WI; see also U.S. patent number 4,937,190) by PCR using primers specific for the 5' and 3' ends of the CITE from nucleotides 16 to 518 in plasmid pCITE4a (the complete sequence of pCITE4a is available at at hypertext transfer protocol world wide web address <http://www.novagen.com/docs/NDIS/69913-000.HTM>). on plasmids pCITE4a-c (Novagen, hypertext transfer protocol world wide web address URL: <http://www.novagen.com>; US patent # 4,937,190); pSLIRES11 (Accession: AF171227; pPV (Accession # Y07702); pSVIRES-N (Accession #: AJ000156); Creancier et al. J. Cell Biol., 10: 275-281 (2000); Ramos and Martinez-Sala, RNA, 10: 1374-1383 (1999); Morgan et al. Nucleic Acids Res., 20: 1293-1299 (1992); Tsukiyama-Kohara et al. J. Virol., 66: 1476-1483 (1992); Jang and Wimmer et al. Genes Dev., 4: 1560-1572 (1990)), or on the dicistronic retroviral vector (Accession #: D88622); or found in eukaryotic cells such as the fibroblast growth factor 2 IRES for stringent tissue-specific regulation (Creancier, et al., J. Cell. Biol., 150:275 (2000)) or the Internal-ribosome-entry-site of the 3'-untranslated region of the mRNA for the beta subunit of mitochondrial H<sup>+</sup>-ATP synthase (Izquierdo and Cuezva, Biochem. J., 346:849 (2000)).

4115-178

At page 9, lines 1-15, please insert the following replacement paragraph:

Non-commercial source of IRES's can also be located. Thus, plasmid pIRES-G (Hobbs,S.M. CRC Centre for Cancer Therapeutics, Institute of Cancer Research, Block F, 15, Cotswold Road, Belmont, Sutton, Surrey SM2 5NG, UK) will serve as source of IRES and the sequence of this plasmid is available (Genebank accession no. Y11034). Furthermore, an Internet search using the NCBI nucleotide database (at hypertext transfer protocol world wide web address <http://www-ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=Display&DB=nucleotide>) and the search parameter "*IRES not patent*" yields 41 Files containing IRES sequences. Finally, IRES cDNA can be made synthetically using an Applied Biosystems ABI™ 3900 High-Throughput DNA Synthesizer (Foster City, CA 94404 U.S.A.), using procedures provided by the manufacturer. To synthesize large IRES sequences such as the 502 bp IRES in pCITE4a, a series of segments are generated by PCR and ligated together to form the full-length sequence using procedures well know in the art [41-43]. Smaller IRES sequences such as the 53 bp IRES in hepatitis C virus (Genebank accession no. 1KH6\_A; [45,46]) can be made synthetically in a single round using an Applied Biosystems ABI™ 3900 High-Throughput DNA Synthesizer (Foster City, CA 94404 U.S.A.) and procedures provided by the manufacturer.

**THE REMAINDER OF THIS PAGE IS INTENTIONALLY LEFT BLANK**